

REMARKS/ARGUMENTS

Claims 1, 2, 6, 7, 27, and 31 to 36 are pending in the application. No claims have been amended, canceled, or added herein.

Applicants respectfully request reconsideration of the rejections of record in view of the following remarks.

The Claimed Subject Matter Would Not Have Been Obvious

Claims 1, 2, 6, 7, 27, and 31 to 36 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 5,804,184 ("the Filpula patent") in view of Takaku, H., *et al.*, *Jpn J Cancer Res* 86: 840-846 (1995) ("the Takaku reference"); Sugimura, K., *et al.*, *Melanoma Res* 2:191-196 (1992) ("the Sugimura reference"); and Oyanagi, K., *et al.*, *Tohoku J Exp Med* 148:385-91 (1986) ("the Oyanagi reference"). Applicants respectfully traverse the rejection because the Office Action has failed to establish *prima facie* obviousness.

To establish *prima facie* obviousness, the PTO must satisfy three requirements. First, the Patent Office must provide objective evidence that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contains some suggestion or incentive that would have motivated those of ordinary skill in the art to modify a reference or to combine references. *In re Lee*, 61 U.S.P.Q.2d 1430, 1433 (Fed. Cir. 2002); *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1998). Second, the proposed modification or combination of the prior art must have had a reasonable expectation of success, determined from the vantage point of those of ordinary skill in the art, at the time the invention was made. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18

U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Finally, the prior art reference or combination of references must teach or suggest all the limitations of the claims. *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

Assuming *arguendo* that those of ordinary skill in the art would have been motivated to combine the teachings of the Filpula patent with those of the Takaku, Sugimura, and Oyanagi references, which Applicants do not concede, the combination fails to teach or suggest every limitation of the claims. The pending claims recite methods for identifying cancer patients susceptible to arginine deprivation therapy comprising obtaining a cancerous tumor sample from the cancer patient and detecting the presence or absence of argininosuccinate synthetase protein in the cancerous tumor sample. In contrast, the Filpula patent, Takaku reference, Sugimura reference, and Oyanagi reference, either alone or in combination, do not disclose, teach, or suggest such methods. For example, the Filpula patent describes arginine deiminase from *Mycoplasma arthritidis*. (Abstract) The patent further describes polymer conjugates of the arginine deiminase and states that the conjugates can be used to treat carcinomas that are deficient in argininosuccinate synthetase. (Col. 9, ln 47 to Col. 10, ln. 57 and Col. 13, Ins. 15 to 18). As acknowledged in the Office Action, the patent fails to teach or suggest methods for identifying cancer patients susceptible to arginine deprivation therapy comprising obtaining a cancerous tumor sample from the cancer patient and detecting the presence or absence of argininosuccinate synthetase protein in the cancerous tumor sample. (Office Action dated July 3, 2003, page 5).

The Takaku, Sugimura, and Oyanagi references similarly fail to teach or suggest such methods. The Takaku reference describes experiments indicating that *Mycoplasma arginini* arginine deiminase inhibited the growth of a mouse hepatoma cell line *in vitro* due to the

depletion of L-arginine. (Page 843-844). The Sugimura reference describes experiments indicating that five melanoma cell lines, but not an epithelial carcinoma cell line, exhibited sensitivity to the growth inhibitory activity of arginine deiminase. (See page 193). The reference further reports that argininosuccinate synthetase mRNA was detected at low levels in the melanoma cell lines. (See pages 193-194). The Oyanagi reference describes the metabolic disorder citrullinemia and reports two case studies in which reduced levels of argininosuccinate synthetase activity were detected in liver tissues of the patients, while normal argininosuccinate synthetase activities were detected in kidney and brain tissues in both cases. The Takaku, Sugimura, and Oyanagi references, whether alone or in combination, fail to teach or suggest methods for identifying cancer patients susceptible to arginine deprivation therapy comprising obtaining a cancerous tumor sample from the cancer patient and detecting the presence or absence of argininosuccinate synthetase protein in the cancerous tumor sample.

A combination of the Filpula patent, the Takaku reference, the Sugimura reference, and the Oyanagi reference, therefore, fails to teach or suggest every limitation of the pending claims. The Office Action has failed to demonstrate otherwise, and, accordingly has failed to establish *prima facie* obviousness. Although the Office Action asserts that the claimed methods "would have been obvious" based upon certain teachings of the cited references, such conclusory statements fall far short of the three requirements that are necessary to establish *prima facie* obviousness. M.P.E.P. § 2142. As discussed above, the Patent Office must provide objective evidence of a suggestion or incentive that would have motivated those of ordinary skill in the art to combine the cited references. Second, the Patent Office must demonstrate that the proposed combination would have had a reasonable expectation of

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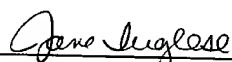
success, determined from the vantage point of those of ordinary skill in the art, at the time the invention was made. Finally, the Patent Office must demonstrate that the combination teaches or suggests all the limitations of the claims. Because the Office Action has failed to meet these requirements, Applicants respectfully request withdrawal of the rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable Action is respectfully requested.

Respectfully submitted,

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